

TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

# 10  
APPLICATION NO. (If known, see 37 CFR 1.5)

INTERNATIONAL APPLICATION NO.  
PCT/US99/04376

INTERNATIONAL FILING DATE  
26 February 1999

PRIORITY DATE CLAIMED  
26 February 1998

TITLE OF INVENTION TWO-DIMENSIONAL LINKAGE STUDY TECHNIQUES

APPLICANT(S) FOR DO/EO/US MCGINNIS, Ralph, Evan MCGINNIS, Robert Owen

Applicant hereby submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☒ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
- a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
- b. ☐ has been transmitted by the International Bureau.
- c. ☒ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
- a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
- b. ☒ have been transmitted by the International Bureau.
- c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
- d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
- ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:

Two signed small entity statements. A signed letter (2 pages long) requesting amendments. 7 Replacement pages, each replacement page with header "PCT/US99/04376(U.S.National Stage Entry Aug. 2000)". Replacement pages are as follows: background replacement page number 5, background replacement page number 6, background replacement page number 7, background replacement page number 8, specification replacement page number 38, specification replacement page number 43, specification replacement page number 46. Express Mail Mailing Certificate, Return Receipt Postcard, Cenwest check for \$48 (small entity Basic National Fee). Statement under Article 19(1).

Copy filed Aug 26, 2000

☒ The following fees are submitted:

**NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :**

Neither international preliminary examination fee (37 CFR 1.482)

nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO

and International Search Report not prepared by the EPO or JPO ..... \$970.00

International preliminary examination fee (37 CFR 1.482) not paid to

USPTO but International Search Report prepared by the EPO or JPO ..... \$840.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but

international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$690.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)

but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... \$670.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)

and all claims satisfied provisions of PCT Article 33(1)-(4) ..... \$96.00

**ENTER APPROPRIATE BASIC FEE AMOUNT =**

\$ 96.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30  
months from the earliest claimed priority date (37 CFR 1.492(e)).

\$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE
Total claims	20 - 20 =	0	X \$18.00
Independent claims	3 - 3 =	0	X \$78.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$260.00

\$

\$

\$

**TOTAL OF ABOVE CALCULATIONS =**

\$ 96.00

Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement  
must also be filed (Note 37 CFR 1.9, 1.27, 1.28).

\$

48.00

**SUBTOTAL =**

\$

48.00

Processing fee of \$130.00 for furnishing the English translation later than ☐ 20 ☐ 30  
months from the earliest claimed priority date (37 CFR 1.492(f)).

\$

+

**TOTAL NATIONAL FEE =**

\$

48.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be  
accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property

\$

+

**TOTAL FEES ENCLOSED =**

\$

48.00

Amount to be

\$

refunded:

charged:

\$

48.00

a. ☒ A check in the amount of \$ 48.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ to cover the above fees.  
A duplicate copy of this sheet is enclosed.

c. ☐ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any  
overpayment to Deposit Account No. \_\_\_\_\_. A duplicate copy of this sheet is enclosed.

**NOTE:** Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Robert Owen McGinnis  
1575 West Kagy Blvd.  
Bozeman, Montana 59715

*Robert O. McGinnis*

SIGNATURE:

Robert O. McGinnis

NAME

44, 232

REGISTRATION NUMBER

(The amendments do not add new matter to the specification. Claims are being cancelled.)

The applicants hereby request the following amendments to the application upon entry into the U.S. National Stage:

**Amendments to the background of the application:**

1) page 5 line 22 after "territory" insert --and that it was difficult to predict the power of using a less dense map at that time--

2) page 5 line 22 after "10" insert -- The inventor's work, however, is a predictor of the power and success of a less dense map.--

A replacement page 5 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect these amendments 1) and 2) to the background.

3) page 6 line 22 after "TDT," change the text "***to increase the likelihood of conditions occurring that increase the power of the TDT in the linkage study, the bi-allelic markers used in the study are chosen so that the least common allele frequencies of the markers vary systematically over a range or subrange of least common allele frequency.***" from bold face italics to regular italics with underlining. A replacement page 6 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect amendment 3) to the background.

4) page 7 line 6 after "TDT," change the text "***to increase the likelihood of both criteria (1) and (2) occurring for one or more markers, so as to increase the power of the TDT in the linkage study, the bi-allelic markers used in the study are chosen so that the least common allele frequencies of the markers vary systematically over a range or subrange of least common allele frequency AND the chromosomal location of the markers vary systematically over one or more chromosomes or chromosomal regions. And the bi-allelic markers are chosen so that the markers' chromosomal locations and least common allele frequencies vary systematically in an essentially independent manner.***" from bold face italics to regular italics with underlining.

5) page 7 line 32 delete the text in brackets [*In addition, the two-dimensional linkage study techniques do not necessarily favor using markers in a scan that are about evenly spaced along a chromosome as in the conventional techniques. This is because* ]. On page 7 line 31 after the text "unfavorably" insert on the insert --Conventional techniques use a one-dimensional concept of "closeness". *These techniques space markers about evenly along a chromosome in the hope that some markers will be "close" (on the chromosome) to the sought gene. (They also favor bi-allelic markers with least common allele frequencies near 0.5.) These--*

A replacement page 7 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect amendments 4) and 5) to the background.

6) page 8 line 18 insert on the next line after "background" -- **Summary**

**Versions of the invention use a new, two-dimensional concept of "closeness" for association-based linkage studies.** Versions of the invention use bi-allelic markers that "cover" or are distributed approximately evenly (or systematically) over two-dimensional regions. These regions have the two dimensions of chromosomal location and least common allele frequency. **Conventional techniques suffer from a kind of one-dimensional lack of depth perception.** (They also favor bi-allelic markers with least common allele frequencies near 0.5.) Two-dimensional linkage study techniques overcome this lack of depth perception. These two-dimensional techniques greatly increase the chance that one or more markers used in a study will be close to the sought gene in two-dimensions. This results in more powerful, systematic and efficient methods (including computer programs) and machines for finding genes, such as harmful

2/2 Letter requesting Amendments to PCT Application PCT/US99/04376 upon 30 month entry into the U.S. National Stage (August 26, 2000)

genes and genes of only modest effect. These techniques also use less dense (more efficient) marker maps (or marker "coverings").

The basic principles behind the two-dimensional approach spawn numerous other inventions. These include methods, machines and compositions of matter (groups of molecules) used for gathering the data (i.e. genotype/sample allele frequency data) used in the new two-dimensional studies, and computer techniques for using and handling such data. These techniques work for creatures other than human beings. And they work for markers and genes that are not bi-allelic (any marker or gene can be mathematically transformed to behave like it is bi-allelic). This summary is not exhaustive or limiting, there are other inventions not listed or specifically described here.--

A replacement page 8 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect amendment 6) to the background.

**Amendments to the Description**

7) page 38 line 2, page 38 line 17 and page 38 line line 20 delete the text "Best Mode" and replace the text "Best Mode" with the text "Set/Subset Example". A replacement page 38 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect the amendments to the description under item 7).

8) page 43 line 4 delete the text "Best Mode" and replace the text "Best Mode" with the text "Set/Subset Example". A replacement page 43 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect the amendment to the description under item 8).

9) page 46 line 24 and line 28 delete the text "Best Mode" and replace the text "Best Mode" with the text "Set/Subset Example". One page 46 lines 26 and 27 delete the text "Best Mode" and replace the text "Best Mode" with the text "Set/Subset". A replacement page 46 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect the amendments to the description under item 9).

**Canceling of Claims and presentation of uncanceled claims for examination**

The applicants hereby request that all claims in the application be cancelled except for the following claims that were filed April 17, 2000: Claims 3, 4, 5, 7, 8, 20, 21, 22, 23, 33, 34, 35, 37, 38, 50, 51, 52, 53, 54, 57. Thus the applicants request that only claims 3, 4, 5, 7, 8, 20, 21, 22, 23, 33, 34, 35, 37, 38, 50, 51, 52, 53, 54, 57 filed April 17 2000 be examined.

I hereby attest that no new matter is added to the specification of the application by the amendments requested in the two pages of this letter.

Respectfully submitted,

Robert McGinnis  
U.S. Patent Agent 44, 232



UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

OCT 05 2001

COMMISSIONER FOR PATENTS  
UNITED STATES PATENT AND TRADEMARK OFFICE  
WASHINGTON, D.C. 20231  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/623,068	08/26/00	MCGINNIS	

HM11/0802

ROBERT MCGINNIS  
1575 WEST KAGY BOULEVARD  
BOZEMAN MT 59715

EXAMINER

HORLICK, K

ART UNIT

PAPER NUMBER

1656

DATE MAILED:

08/02/01

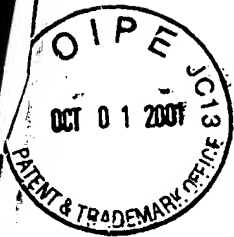
Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment filed on 6/25/01 is considered non-compliant because it has not been submitted in the format required under 37 CFR 1.121, as amended on September 8, 2000 (see 65 Fed. Reg. 54603, Sept. 8, 2000, and 1238 O.G. 77, Sept. 19, 2000).

- ☒ 1. The amendment does not include a clean version of the replacement paragraph(s)/section(s). 37 CFR 1.121(b)(1)(ii).
  - ☐ 2. The amendment does not include a marked-up version of the replacement paragraph(s)/section(s). 37 CFR 1.121(b)(1)(iii).
  - ☒ 3. The amendment does not include a clean version of the amended claim(s). 37 CFR 1.121(c)(1)(i).
  - ☐ 4. The amendment does not include a marked-up version of the amended claim(s). 37 CFR 1.121(c)(1)(ii).
  - ☐ 5. Other \_\_\_\_\_
- ☐ **PRELIMINARY AMENDMENT:** Unless applicant re-submits the preliminary amendment in compliance with revised 37 CFR 1.121 within ONE MONTH of the mail date of this letter, examination on the merits may commence without entry of the originally proposed preliminary amendment. This notice is not an action under 35 U.S.C. 132, and this ONE MONTH time limit is not extendable.
- ☐ **AMENDMENT AFTER NON-FINAL ACTION:** Since the above mentioned reply appears to be *bona fide*, applicant is given a TIME PERIOD of ONE (1) MONTH or THIRTY (30) DAYS from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

For your convenience, attached to this correspondence is a copy of an informational flyer (MPEP Bookmark Bulletin on "Simplified Amendment Practice").

*Helen G. Hamner*  
Legal Instruments Examiner



**Express Mail Certificate for Amendment Response to Notice of Non-Compliant Amendment (37 CFR 1.121) for Application No. 09/623, 068.**

The following items have been deposited with US Express Mail today Oct , 2001, addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231. Express Mail Label. **EK751372172US**

- 1) Amendment/Response 10 pages
- 2) List of Acronyms used in genome research 14 pages.
- 3) Copy of Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a filing under 35 USC 371, filed with PCT/US99/04376 (matured into US National Stage application No. 09/623, 068) on 8/26/2000 on Entry into US National Stage. 2 pages
- 4) Copy of Letter requesting Amendments to PCT Application PCT/US99/04376 upon 30 month entry into US National Stage. 2 pages
- 5) Two return receipt post cards.
- 6) Petition for Extension of Time for 1 month under 37 CFR 1.136 (a) with enclosed fee \$55 (small entity) by check, First Interstate Bank number 513
- 7) Copy of Notice of Non-Compliant Amendment (37 CFR 1.121)

Deposited by me with US Mail today, Oct 1 , 2001.

*Robert McGinnis*

Robert McGinnis, Registration No. 44,232